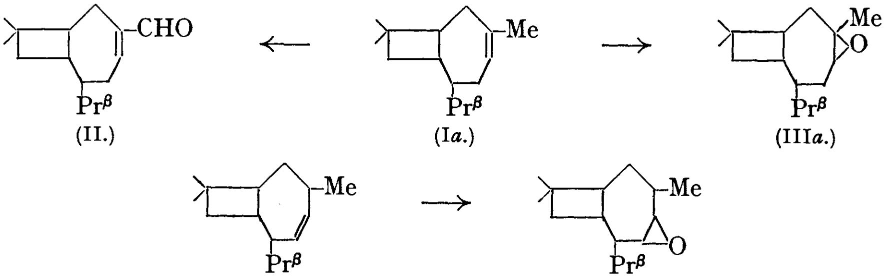
121. *The Constitution of Caryophyllene. Part II. Oxidation Reactions of Caryophyllene and Dihydrocaryophyllene.*

By H. N. Rydon.

Dihydrocaryophyllene has been oxidised with selenious acid to *dihydrocaryophyllene aldehyde*, and with perbenzoic acid to two isomeric *dihydrocaryophyllene oxides*. Oxidation of caryophyllene with selenious acid gave only resinous products, but oxidation with perbenzoic acid yielded *caryophyllene oxide*. A further piece of evidence from the literature for the new caryophyllene structure advanced in Part I (*Chem. and Ind.*, 1938, **57**, 123) is discussed.

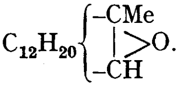
The publication of a paper by Triebs (*Ber.*, 1939, **72**, 7) referring, without experimental details, to the production of an oxide from caryophyllene has made it desirable to put on record some of the results obtained in experiments on the oxidation of caryophyllene and dihydrocaryophyllene having as their object the testing of the validity of the structure put forward in Part I.

The action of selenious acid in boiling butyl alcohol on caryophyllene did not give promising results and attention was turned to its action on dihydrocaryophyllene obtained by catalytic hydrogenation of caryophyllene : the structure of Part I being adopted, the dihydrocaryophyllene was probably a mixture of two isomers, (I*a*) and (I*b*), derived from the two non-conjugated caryophyllene isomers and the conjugated isomer, respectively.


(II.) (I*a*.) (III*a*.)

(I*b*.) (III*b*.)

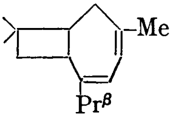
The oxidation gave a fair yield of an aldehyde, $C_{15}H_{24}O$, which is regarded as *dihydrocaryophyllene aldehyde* (II), oxidation having taken place preferentially at the methyl group (cf. pinene ⟶ myrtenal; Dupont, Zacharewicz, and Dulon, *Compt. rend.*, 1934, **198**, 1699). By selenium dioxide oxidation of caryophyllene in acetic anhydride Treibs (*Ber.*, 1938, **71**, 1794) obtained a poor yield of the acetate of a primary alcohol derived by oxidation of the same methyl group. Further oxidative degradation of dihydrocaryophyllene aldehyde has so far not led to any positive result.

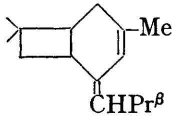
Caryophyllene reacted readily with perbenzoic acid in chloroform, affording a *caryophyllene oxide* in 70% yield. By analogy with limonene, in which the double bond more resistant to hydrogenation reacts preferentially with perbenzoic acid (Meerwein, *J. pr. Chem.*, 1926, **113**, 9), this is regarded as a mixture of three double-bond isomers of the type  $C_{12}H_{20}\left\{\begin{array}{l}-CMe\\ \mid >O\\ -CH\end{array}\right.$. A further oxide derived from the conjugated isomer is not to be expected, since isoprene gives only one oxide with perbenzoic acid (Pummerer and Reindel, *Ber.*, 1933, **66**, 335). It has not so far been found possible to open the oxide ring smoothly.

Dihydrocaryophyllene also reacted readily with perbenzoic acid in chloroform solution. The product was a readily separable mixture (yield 70%) of two isomeric oxides, fractionation yielding *dihydrocaryophyllene* α-*oxide*, b. p. 134—137°/12 mm., $\alpha_D^{20^\circ}$ − 3·38°, and *dihydrocaryophyllene* β-*oxide*, b. p. 145—147°/12 mm., $\alpha_D^{20^\circ}$ − 4·46°. The formation of these two isomers leaves little doubt that dihydrocaryophyllene is a mixture; they are assigned the structures (III*a*) and (III*b*), the latter probably representing the β-oxide, which was formed in smaller amount. Neither of these two oxides has so far been smoothly converted into a glycol.

All the above results are equally capable of explanation on similar lines on the basis of Ruzicka's structure for caryophyllene (V; for the conjugated isomer) (*Chem. and Ind.*, 1935, **54**, 509).

(IV.)





(V.)

Caryophyllene readily forms a crystalline adduct with maleic anhydride (Ruzicka and Zimmermann, *Helv. Chim. Acta*, 1935, **18**, 219), doubtless derived from the conjugated isomer, (IV) or (V), both pre-existing in the sesquiterpene mixture and formed from the corresponding *iso*propylidene isomer by double-bond migration during the reaction. Now Goodway and West have shown (J., 1938, 2028) that, whereas α-phellandrene, which contains a *cis*-butadiene system as does (IV), reacts normally and readily with maleic anhydride, β-phellandrene, which contains a *trans*-butadiene system as does (V), gives only a poor yield of amorphous material; this appears to be a further piece of evidence in favour of the new structure for caryophyllene.

An attempt to obtain a glycol from dihydrocaryophyllene by Meerwein's method (D.R.P. 574,838) was fruitless. Preliminary experiments on the autoxidation of caryophyllene have given promising results and the work is being actively pursued along these lines.

EXPERIMENTAL.

Caryophyllene obtained by redistillation of the commercial product had b. p. 119—121°/11 mm., $n_{\mathrm{D}}^{16^\circ}$ 1·5009, $\alpha_{\mathrm{D}}^{16^\circ}$ − 8·52° (Ruzicka and Wind, *Helv. Chim. Acta*, 1931, **14**, 410, give b. p. 119—121°/12 mm., $n_{\mathrm{D}}^{16^\circ}$ 1·5009, α_{D} − 8·9°).

Dihydrocaryophyllene.—Caryophyllene (51 g.) in absolute alcohol (100 c.c.) was shaken in hydrogen at 3—4 atms. in the presence of 2% palladised strontium carbonate (2·5 g.); 1 g.-mol. of hydrogen was absorbed in 6—8 hours. The product (48 g.), isolated in the usual way, had b. p. 120—122°/13 mm., $n_{\mathrm{D}}^{15^\circ}$ 1·4908, $\alpha_{\mathrm{D}}^{15^\circ}$ −23·84° (Deussen, *J. pr. Chem.*, 1926, **114**, 63, gives $n_{\mathrm{D}}^{18^\circ}$ 1·4885, α −25°; *idem, Annalen*, 1912, **388**, 156 : $n_{\mathrm{D}}^{20^\circ}$ 1·4903, α −24·0°).

Oxidation of Caryophyllene with Selenious Acid.—A solution of 10 g. of caryophyllene in 40 c.c. of butyl alcohol was treated with 6·5 g. of powdered selenious acid. A vigorous reaction set in at the b. p.; after this had abated, refluxing was continued for 5 hours. The precipitated selenium was filtered off and washed with alcohol; evaporation of the filtrate yielded a resin which gave no ketonic reactions and was not further examined.

Oxidation of Dihydrocaryophyllene with Selenious Acid.—48 G. of dihydrocaryophyllene were dissolved in 125 c.c. of butyl alcohol, and 26 g. of powdered selenious acid added. After the vigorous reaction which set in at the b. p. had abated, the mixture was refluxed for 6 hours. The precipitated selenium was removed from the cooled solution, and the filtrate distilled. The product (29 g.; 57%), b. p. 145—158°/12 mm., was still impure and contained selenium, although it gave a very good yield of semicarbazone. A solution in 150 c.c. of light petroleum (b. p. 40—60°) was run through a column of Brockmann alumina and washed through with a further 150 c.c. of petroleum. Recovery of the material from the filtrate gave *dihydrocaryophyllene aldehyde* (II) (18·5 g.; 36%) as a pale yellow oil with an odour of camphor and cedar-wood, b. p. 157—160°/15 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5073 (Found: C, 81·6; H, 10·9. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%); the substance gave a strongly positive Schiff reaction and quickly formed a sticky polymer or oxidation product on keeping. The *semicarbazone* formed stellate clusters of prismatic needles from dilute alcohol, m. p. 242° (Found : N, 15·25. $C_{16}H_{27}ON_3$ requires N, 15·2%); it was of no value for purification, as regeneration was very difficult.

Oxidation of Caryophyllene with Perbenzoic Acid.—17 G. of caryophyllene were added to a solution of perbenzoic acid in chloroform (270 c.c.) containing 1·34 g. of available oxygen. The solution, which became hot, was cooled in ice and the reaction was followed by iodometric titration. After 30 minutes the titre had fallen to zero and the solution was washed twice with 10% sodium hydroxide solution and then with water. Distillation of the dried solution gave 13 g. (71%) of *caryophyllene oxide* as a thick colourless oil, b. p. 138—141°/10 mm., $n_{\mathrm{D}}^{14^\circ}$ 1·4987 (Found : C, 81·2; H, 10·8. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%).

Oxidation of Dihydrocaryophyllene with Perbenzoic Acid.—27 G. of dihydrocaryophyllene were added to a solution of perbenzoic acid in 295 c.c. of chloroform containing 2·12 g. of available oxygen. The solution became warm and was cooled in ice. Titration showed 90% reaction in 30 minutes and 95% reaction in 2½ hours. The solution was then washed successively with sodium iodide solution, sodium hydroxide solution, and water. Distillation of the dried solution gave 12 g. (41%) of *dihydrocaryophyllene α-oxide* (III*a*) as a colourless, sweet-smelling oil, b. p. 134—137°/12 mm., $n_{\mathrm{D}}^{18^\circ}$ 1·4806, $\alpha_{\mathrm{D}}^{20^\circ}$ − 3·38° (Found : C, 81·3; H, 11·9. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%), and 8 g. (28%) of *dihydrocaryophyllene β-oxide* (III*b*), a colourless, almost odourless oil, b. p. 145—147°/12 mm., $n_{\mathrm{D}}^{18^\circ}$ 1·4832, $\alpha_{\mathrm{D}}^{20^\circ}$ − 4·46° (Found: C, 80·8; H, 11·8%).

Meerwein Oxidation of Dihydrocaryophyllene.—19 G. of dihydrocaryophyllene were cooled in ice-water and stirred mechanically while a cooled mixture of 11 c.c. of acetic acid, 1·2 g. of sulphuric acid, and 11 c.c. of 30% hydrogen peroxide was added during 1½ hours. Stirring was continued for 68 hours, at first at 0° but later at room temperature. After heating on the water-bath for 30 minutes, the product was treated with 10% sodium hydroxide solution and extracted with ether. The residue from the dried extract was refluxed on the water-bath for 48 hours with 10 g. of potassium hydroxide, 10 c.c. of water, and 100 c.c. of ethyl alcohol. The alcohol was removed in a vacuum, and the residue steam-distilled to remove volatile matter. The product was an intractable plastic mass which refused to crystallise.

The author thanks the Royal Society for a grant and the Royal Commissioners for the Exhibition of 1851 for a Senior Studentship.

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